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EXAMINER

EWOLDT, GERALD R

ART UNIT

PAPER NUMBER

1644

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25

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/267,456

Applicant(s)

Mosca et al.

Examiner

G.R. Ewoldt

Art Unit

1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 12/4/02 and 3/4/03
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 21-36 is/are pending in the application.
- 4a) Of the above, claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 21-36 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claims \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some\* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\*See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).  
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). \_\_\_\_\_ 6) ☐ Other:

#### DETAILED ACTION

1. A request for continued examination (RCE) under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. The amendment and remarks, filed 12/04/02, have been entered.

2. Claims 17-20 have been canceled.  
Claims 21-36 are pending and being acted upon.

3. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Newly added Claims 21-36 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Specifically, the specification provides insufficient evidence that after contacting mesenchymal stem cells (MSCs) *in vitro* with an antigen, the MSCs of the claimed method would process said antigen into an antigen fragment for presentation by said MSCs, for the reasons of record as set forth in Papers No. 17 and 20, mailed 2/28/02 and 9/19/02, respectively.

Applicant's arguments, filed 12/04/02, have been fully considered but they are not persuasive. Applicant argues that the Janeway et al. reference, upon which the rejection was based in part, was published in 1994. Subsequent publications of an abstract by Keane-Moore et al. (1998) and U.S. Patent No. 6,149,906 (priority date 1997) are submitted in support of the method of the instant claims.

Applicant argues that the Keane-Moore et al. reference teaches that hMSCs transduced with B7-1 or B7-2 successfully presented tetanus toxoid to a T cell line and the '906 patent teaches that interferon-gamma (IFN $\gamma$ ) treated hMSCs can be effective antigen presenting cells in order to induce a T cell

response.

The Examiner concedes all of these arguments. However, none of these arguments address the basis of the rejection, i.e., that the specification fails to demonstrate antigen processing. Regarding the age of the Janeway et al. reference, Applicant is advised that a reference published subsequent to Keane-Moore et al. or the priority date of the '906 patent, is herewith provided that still fails to recognize MSCs as APCs (Paul, ed., *Fundamental Immunology*, 1999). Accordingly, any specific properties regarding the antigen presentation capability of MSCs, e.g., antigen processing, are highly unexpected and therefore highly unpredictable.

Applicant asserts that Example 1 of the instant specification demonstrated that MSCs can be pulsed with antigen and that said antigen is then presented to T cells in order to induce tolerance. Applicant concludes with the assertion that "Thus, Applicants' discovery is not of such a speculative; abstruse or esoteric nature that it must be considered unbelievable, incredible, or factually misleading," and "The Examiner, therefore, has not met his burden in showing that the specification does not provide an enabling disclosure."

It is the Examiner's position that no claims are drawn to T cell tolerance, thus, the first assertion is irrelevant. Regarding Applicant's asserted "discovery", neither the specification, the prior art, nor the instant arguments provide any evidence that antigens are processed. Accordingly, claims drawn to antigen processing must be considered unpredictable for the reasons of record and the following reasons.

The Keane-Moore et al. reference and Example 1 of the '906 patent demonstrate that IFN $\gamma$  treated hMSCs can be induced to express MHC Class II. The references are silent, however, regarding antigen processing. Antigens can be pulsed (or loaded) onto APCs without antigen processing. Indeed, pulsed antigens generally simply replace the antigens found in surface MHCs due to high concentration in the media in which the APCs are pulsed. At issue here is really whether or not hMSCs have the specialized antigen processing machinery found in APCs. See again Paul, ed., *Fundamental Immunology*, 1999 (Figure 1, page 268), in which it is shown that highly specialized endosomes, lysosomes and antigen processing molecules such as CLIP are required for antigen processing. It remains the Examiner's position that no demonstration of this highly specialized machinery being present in MSCs has been presented, and given the fact that nowhere in

the prior art of record has it been shown that MSCs possess the machinery that one of skill in the art would only expect to find in APCs, one of skill in the art would find the method of the instant claims highly unpredictable.

5. The following is a new ground of rejection.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:


The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 21-36 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted step is a pretreatment of the hMSCs with IFN $\gamma$ . The instant specification discloses that pretreatment of the hMSCs with IFN $\gamma$  is optional. Both the Keane-Moore et al. reference and Example 1 of the '906 patent teach that pretreatment of the hMSCs with IFN $\gamma$  is required for the upregulation of MHC Class II. Accordingly, said step is considered to be essential and must be recited in the claims.

8. No claim is allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (703) 308-9805. The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 at 703-872-9306 (before final) and 703-872-9307 (after final).

  
G.R. Ewoldt, Ph.D.  
Primary Examiner  
Technology Center 1600  
April 24, 2003